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PII: S1413-8670(21)00089-1
DOI: <https://doi.org/10.1016/j.bjid.2021.101620>
Reference: BJID 101620



To appear in: *Brazilian Journal of Infectious Diseases*

Received date: 11 May 2021
Accepted date: 25 August 2021

Please cite this article as: Lisiane F. Leal , Joanna Merckx , Deshayne B. Fell , Ricardo Kuchenbecker , Angelica E. Miranda , Wanderson K. de Oliveira , Robert William Platt , Lívia Antunes , Mariângela F. Silveira , Natália Bordin Barbieri , Characteristics and outcomes of pregnant women with SARS-CoV-2 infection and other severe acute respiratory infections (SARI) in Brazil from January to November 2020, *Brazilian Journal of Infectious Diseases* (2021), doi: <https://doi.org/10.1016/j.bjid.2021.101620>

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Characteristics and outcomes of pregnant women with SARS-CoV-2 infection and other severe acute respiratory infections (SARI) in Brazil from January to November 2020

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Abstract

Background: Knowledge about COVID-19 in pregnancy is limited, and evidence on the impact of the infection during pregnancy and postpartum is still emerging.

Aim: To analyze maternal morbidity and mortality due to severe acute respiratory infections (SARI), including COVID-19, in Brazil.

Methods: National surveillance data from the SIVEP-Gripe (*Sistema de Informação de Vigilância Epidemiológica da Gripe*) was used to describe currently and recently pregnant women aged 10-49 years hospitalized for SARI from January through November, 2020. SARI cases were grouped into: COVID-19; influenza or other detected agent SARI; and SARI of unknown etiology. Characteristics, symptoms and outcomes were presented by SARI type and region. Binomial proportion and 95% confidence intervals (95% CI) for outcomes were obtained using the Clopper-Pearson method.

Results: Of 945,460 SARI cases in the SIVEP-Gripe, we selected 11,074 women aged 10-49 who were pregnant (7,964) or recently pregnant (3,110). COVID-19 was confirmed in 49.4% cases; 1.7% had influenza or another etiological agent; and 48.9% had SARI of unknown etiology. The *pardo* race/ethnic group accounted for 50% of SARI cases. Hypertension/Other cardiovascular diseases, chronic respiratory diseases, diabetes, and obesity were the most common comorbidities. A total of 362 women with COVID-19 (6.6%; 95%CI 6.0-7.3) died. Mortality was 4.7% (2.2-8.8) among influenza patients, and 3.3% (2.9-3.8) among those with SARI of unknown etiology. The South-East, Northeast and North regions recorded the highest frequencies of mortality among COVID-19 patients.

Conclusion: Mortality among pregnant and recently pregnant women with SARIs was elevated among those with COVID-19, particularly in regions where maternal mortality is already high.

Keywords: Pregnancy; Maternal mortality; Severe acute respiratory infections; SARS-CoV-2; Brazil; SIVEP-Gripe

Introduction

By November 23, 2020, Brazil had more than six million confirmed cases of COVID-19 and 176,000 associated deaths.¹ These numbers are likely underestimates. According to the Epicovid19-BR, a national serological household population-based survey, for each confirmed diagnosis, there are approximately six additional unreported cases, and for every 100 hundred infected, one dies.² In addition, ethnic and regional disparities in rates of infection have been documented in Brazil.³

Evidence about the impact of COVID-19 during pregnancy and postpartum is still emerging. Early case series studies from China suggested that pregnant women were not at increased risk of severe disease.⁴ However, as the pandemic spread globally, evidence of increased clinical severity, including mortality, among pregnant women emerged in some high-income countries.⁵⁻⁷

Knowledge about the impact of COVID-19 during pregnancy in low- and middle-income countries (LMIC) is limited. A recent study of 978 pregnant and postpartum Brazilian women with COVID-19 reported 124 deaths (case fatality rate of 12.7%) by June 18, 2020. Risk factors for mortality among these cases, included obesity, diabetes, cardiovascular diseases, and postpartum period.⁸ However, no information has been reported on maternal morbidity and mortality from other/unknown severe acute respiratory illnesses (SARIs) during the same period, even though SARIs with unknown etiology have increased in Brazil since the beginning of the pandemic, and may actually reflect undiagnosed COVID-19.⁹ Understanding the treatment and clinical outcomes of pregnant and recently pregnant women with COVID-19 and other SARIs is needed to inform public health decision-making.

This manuscript analyzes maternal morbidity and mortality due to SARIs, including COVID-19, in Brazil, using data from the SIVEP-Gripe (*Sistema de Informação de Vigilância Epidemiológica da Gripe*) for January to November 2020.

Methods

Data source

The development of Brazilian reporting systems for surveillance of the COVID-19 pandemic has been described elsewhere.^{3,9,10} Briefly, in January 2020, the Ministry of Health implemented a REDCap platform to prospectively report suspected, probable and confirmed COVID-19 cases. By March, the REDCap system had been discontinued and mild COVID-19 cases began to be reported on e-SUS *Vigilância Epidemiológica* (e-SUS-VE), a new national COVID-19 reporting system. Meanwhile, hospitalized COVID-19 cases were recorded on the SIVEP-Gripe, which had been created in 2002 and used for surveillance of circulating viruses. In 2009, this system incorporated SARI notification for all hospitals, and has since been used to report SARIs in the Brazilian population. Both e-SUS-VE and SIVEP-Gripe include suspected and confirmed COVID-19 cases as reported by public and private health services. The two systems are inter-related on the Brazilian Ministry of Health "Portal do COVID-19" website (<https://covid.saude.gov.br/>), which summarizes daily aggregated counts from both platforms.⁹

All SARI-related hospital admissions and deaths are captured in the SIVEP-Gripe, and notifications are mandatory. The SIVEP-Gripe records variables, such as notification date, onset of symptoms, hospitalization, collection of clinical specimens, detection, release of laboratory results, and case resolution (Supplementary Table S1). Access to de-identified and unduplicated data is publicly available (<https://opendatasus.saude.gov.br/dataset/bd-srag-2020>).¹¹

Study design and population

This population-based case series study used surveillance data from the SIVEP-Gripe. We included all cases of currently and recently pregnant women aged 10-49 years, who were hospitalized because of SARIs (including COVID-19) between January 1 and November 23, 2020. Currently pregnant women were identified as those with a recorded gestational age, who were not simultaneously recorded as postpartum nor had had an abortion. Recently pregnant women comprised those in the postpartum or post-abortion period. Those for whom final classification of the case (final diagnosis by type of SARI) was missing were excluded.

Measures

SIVEP-Gripe classifies SARI cases as being due to influenza, other respiratory virus, other etiological agents, COVID-19, or with unknown etiology.¹² We regrouped SARI cases into three categories:

- COVID-19, defined as SARS-CoV-2 infection confirmed by laboratory testing (molecular diagnostics with real-time quantitative PCR or serology), clinical/epidemiological, clinical or clinical-imaging criteria;
- Influenza or other detected agent SARI, defined by a laboratory-confirmed respiratory virus or other etiological infectious agent; and
- SARI with unknown etiology, defined by clinically-confirmed influenza-like illnesses or SARI with no etiologic agent identified.

Maternal age was computed by the SIVEP-Gripe as the interval between the woman's date of birth and date of the first symptoms, and was categorized as: 10 to 19, 20 to 29, 30 to 39, and 40 to 49 years.

Race/ethnicity was recorded according to the patient's declaration. The official Brazilian classification recognizes five groups: *branco* (White), *pardo* (those who declare themselves as such or as mulatto, *cabocla*, *cafuzo*, *mameluca* or *mestizo*), *preto* (Black), *amarelo* (East Asian), and *indígena* (Indigenous).

Education was the highest grade/year the patient declared, and was grouped into five categories: no education; elementary; high school; higher education; and missing or unknown.

Results are presented by region of residence and federation unit (state level). The regional division of Brazil consists of states (26 states and the Federal District) and municipalities grouped into five regions (North, Northeast, Southeast, South, and Central West).

We adapted the World Health Organization list of signs and symptoms and comorbidities available in the COVID-19 Data Platform for monitoring pregnancies.¹³ Hypertension (pre-existing or onset during pregnancy) is grouped with other cardiovascular diseases. Diabetes is a composite variable including pre-existing and gestational diabetes.

Outcomes (admission to intensive care unit [ICU], ventilatory support, and death) are presented by SARI type and region of residence.

The supplemental material contains additional details for coding of study variables (Supplementary Table S2).

Statistical analysis

We used descriptive statistics to summarize the characteristics of the study population. Categorical variables are summarized as counts and percentages; continuous variables are expressed as medians with inter-quartile ranges. Binomial proportion and 95% confidence intervals (95% CI) for outcomes were obtained using the Clopper-Pearson method. Analyses were performed with SAS software, version 9.4 (SAS Institute, Inc., Cary, North Carolina). We used ArcGIS, version 10.6, (Environmental Systems Research Institute, Redlands, WA, USA) to plot the number of cases and deaths by region of residence. To construct maps, we used the Natural Breaks (Jenks) method for defining ranges and consolidation of classes.

Ethical statement

This study used only non-identifiable publicly available data; therefore, no ethical approval was necessary.

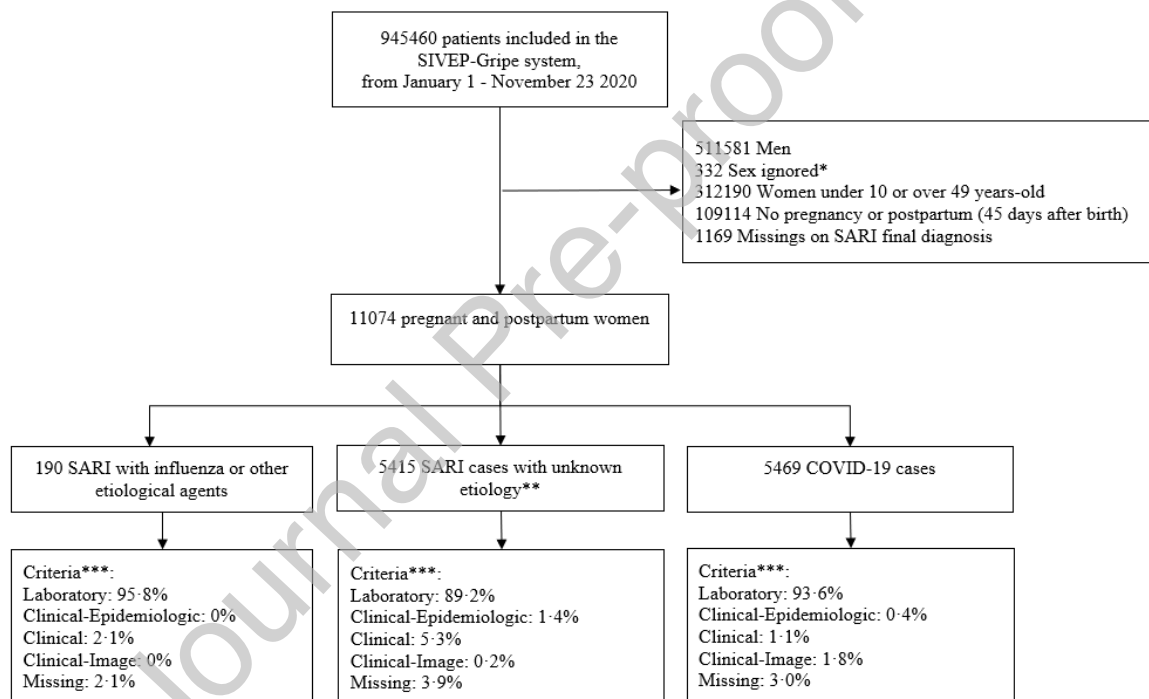
Results

Among 945,460 cases of SARI hospitalized between January 1 and November 23, 2020, 11,074 (1.2%) were pregnant or recently pregnant women and constituted the study population. Of these 11,074 women, 71.9% were currently pregnant (including those with trimester missing information), and 28.1% were recently pregnant.

Close to half (49.4%) were confirmed COVID-19 cases, and 48.9% had SARI of unknown etiology; the remaining 1.7% had confirmed influenza or another etiological agent.

Figure 1 presents the flow diagram for identifying the study population.

Figure 1. Study flow diagram.



Dataset: 23-11-2020

Abbreviation: SARI=Severe Acute Respiratory Infection; SIVEP-Gripe=Sistema de Informação de Vigilância Epidemiológica da Gripe

*Sex ignored is one of the categories allowed for recording this variable, it does not mean missing.

**SARI case for which no other etiologic agent was identified OR it was not possible to collect / process clinical sample for laboratory diagnosis, OR it was not possible to confirm by clinical-epidemiological, clinical-image or clinical criteria.

***Criterion used for final classification of the case.

Current case definition: <https://coronavirus.saude.gov.br/definicao-de-caso-e-notificacao>

Forty-four percent of these women were aged 20-29, and 37% were aged 30-39 (Table 1). Almost half (45.9%) reported *pardo* race/ethnicity, although about 20% of records were missing information on ethnic origin.

Table 1. Characteristics of pregnant and recently pregnant women with SARI infections who were admitted or died, SIVEP-Gripe, Brazil, January-November 2020 (n=11,074)

Characteristics	SARI with influenza or other etiological agents (n=190)		SARI cases with unknown etiology (n=5,415)		COVID-19 cases (n=5,469)	
	n	%	n	%	n	%
Age (years), median (IQR)	27	21;32	27	22;33	29	24;34
Age group (years)						
10 to 19	33	17.4	836	15.4	534	9.8
20 to 29	82	43.2	2,494	46.1	2,267	41.4
30 to 39	70	36.8	1,766	32.6	2,264	41.4
40 to 49	5	2.6	319	5.9	404	7.4
Race/ethnicity (self-reported)						
White	75	39.5	1,597	29.5	1,404	25.7
Black	12	6.3	401	7.4	281	5.1
East Asian	2	1.0	40	0.7	46	0.8
Pardo	78	41.0	2,374	43.8	2,633	48.1
Indigenous	0	0	30	0.6	80	1.5
Missing/unknown	23	12.1	973	18.0	1,025	18.7
Education level						
No education	1	0.5	23	0.4	17	0.3
Elementary school	38	20.0	865	16.0	704	12.9
High school	56	29.5	1,229	22.7	1,316	24.1
Higher education	22	11.6	314	5.8	409	7.5
Missing/unknown	73	38.4	2,984	55.1	3,023	55.3
Comorbidities						
Hypertension/other cardiovascular disease	14	7.4	522	9.6	562	10.3
Diabetes	8	4.2	292	5.4	421	7.7
Asthma/other chronic lung diseases	14	7.4	513	9.5	241	4.4
Obesity	7	3.7	185	3.4	264	4.8
Immunosuppression/HIV	3	1.6	114	2.1	69	1.3
Chronic hematological diseases or anemia	1	0.5	77	1.4	56	1.0
Neurological disease or depression	3	1.6	58	1.1	47	0.9
Chronic renal disease	0	0	47	0.9	46	0.8
Chronic liver disease or hepatitis	0	0	29	0.5	17	0.3
Tuberculosis	0	0	10	0.2	2	0.04
Other comorbidities	12	6.3	274	5.1	238	4.3
Smoking (former or current)	5	2.6	79	1.5	19	0.3
Gestational age						
First trimester	16	8.4	531	9.8	378	6.9
Second trimester	48	25.3	1,102	20.3	985	18.0
Third trimester	86	46.3	1,914	35.3	2,475	45.3

Trimester ignored	9	4.7	182	3.4	238	4.3
Postpartum or post-abortion	31	16.3	1,686	31.1	1,393	25.5
Imaging (X-ray or CT)						
Not performed	69	36.3	2,078	38.4	2,039	37.3
Performed	64	33.7	1,519	28.0	1,596	29.2
Missing/unknown	57	30.0	1,818	33.6	1,834	33.5
Region of residence*						
Southeast	58	30.5	2,412	44.5	1,852	33.9
Northeast	56	29.5	1,487	27.5	1,668	30.5
Central-West	26	13.7	487	9.0	701	12.8
North	12	6.3	360	6.6	792	14.5
South	38	20.0	669	12.3	454	8.3

* Two missings on region not computed here.

Overall, hypertension or other cardiovascular diseases, chronic respiratory diseases, diabetes, and obesity were the most common comorbidities in this population (9.9%, 6.9%, 6.5%, and 4.1%, respectively). Among those with COVID-19, hypertension/other cardiovascular disease and diabetes were the leading comorbidities (10.3% and 7.7%, respectively). Asthma/other lung diseases was the most common comorbidity among those with influenza-associated SARI (7.5%) and among those with SARI of unknown etiology (9.5%).

Four in ten (40.4%) women in the study population were in their third trimester, and 28.1% were in the postpartum or post-abortion period. Recorded abortions accounted for 0.7% of recently pregnant patients.

Based on absolute case counts, the highest burden of disease was in the Southeast region with 39.0% of the total number of SARI cases, followed by the Northeast (29.0%), Central-West (11.0%, North (10.5%), and South (10.5%). The Southeast and Northeast regions reported the highest percentages of COVID-19 cases (33.9% and 30.5%, respectively).

A large majority (93.4%) of the SARI cases were recorded as symptomatic; 1.3% had no symptoms; and 4.8% had missing information for all variables related to symptoms. Cough was the most frequently recorded symptom (64.8%), regardless of SARI type (Table 2). Compared with the other groups, those with COVID were more likely to have loss of smell or taste, headache, diarrhea, fatigue/malaise, and muscle aches. Fever, cough, sore throat, and oxygen saturation <95% were relatively more frequent among those with SARI with influenza or another etiological agent.

Table 2. Signs and symptoms of pregnant and recently pregnant women with SARI infections who were admitted or died, SIVEP-Gripe, Brazil, January-November 2020 (n=11,074)

Signs and symptoms	SARI with influenza or other etiological agents (n=190)		SARI cases with unknown etiology (n=5,415)		COVID-19 cases (n=5,469)	
	n	%	n	%	n	%
Symptomatic cases, n (%)	190	100	5,159	95.3	5,048	92.3
Fever	134	70.5	2,727	50.4	3,107	56.8
Cough	162	85.3	3,466	64.0	3,550	64.9
Sore throat	80	42.1	1,122	20.7	1,180	21.6
Shortness of breath	113	59.5	2,541	46.9	2,593	47.4
Oxygen saturation < 95%	61	32.1	1,281	23.7	1,351	24.7
Vomiting or nausea	22	11.6	637	11.8	557	10.2
Runny nose or nasal congestion	20	10.5	567	10.5	566	10.3
Headache	22	11.6	592	10.9	828	15.1
Muscle aches	18	9.5	384	7.1	731	13.4
Diarrhea	13	6.8	473	8.7	545	10.0
Fatigue/malaise	12	6.3	352	6.5	503	9.2
Loss of smell	2	1.0	214	3.9	850	15.5
Loss of taste	3	1.6	156	2.9	565	10.3
Chest pain	3	1.6	104	1.9	107	2.0
Abdominal pain	6	3.2	189	3.5	181	3.3
Joint pain (arthralgia)	0	0	18	0.3	18	0.3
Conjunctivitis	0	0	6	0.1	1	0.02
Skin rash or skin ulcers	0	0	9	0.2	8	0.1
Bleeding (hemorrhage)	0	0	6	0.1	12	0.2
Lymphadenopathy	0	0	2	0.04	2	0.04
Other symptoms	15	7.9	366	6.8	337	6.2

Maternal outcomes by SARI type are described in Table 3. ICU admission was more frequent in women with COVID-19 (19.5%; 95%CI: 18.4-20.5) than among those with SARI of unknown etiology (16.8%; 95%CI: 15.8-17.8) or influenza (15.8%; 95%CI: 10.9-21.8). For those admitted to ICU, the length of stay for COVID-19 cases was longer (median of 6 days) than that for women with other SARIs. Most women (56.7%) did not receive invasive ventilatory support.

Table 3. Hospital outcomes among pregnant and recently pregnant women with SARI infections, SIVEP-Gripe, Brazil, January-November 2020 (n=11,074)

Maternal outcomes	SARI with influenza or other etiological agents (n=190)			SARI cases with unknown etiology (n=5,415)			COVID-19 cases (n=5,469)		
	n	%	(95% CI)*	n	%	(95% CI)*	n	%	(95% CI)*
Admission to intensive care unit (ICU)	30	15.8	(10.9-21.8)	911	16.8	(15.8-17.8)	1,065	19.5	(18.4-20.5)
ICU length of stay, median (IQR)		4	(1;7)		3	(2;6)		6	(3;13)
Ventilatory support									
Not artificially ventilated	110	57.9	(50.5-65.0)	3,142	58.0	(56.7-59.3)	3,022	55.3	(53.9-56.6)
Invasive ventilation	14	7.4	(4.1-12.0)	344	6.3	(5.7-7.0)	455	8.3	(7.6-9.1)
Non-invasive ventilation	42	22.1	(16.4-28.7)	1,144	21.1	(20.0-22.2)	1,223	22.4	(21.3-23.5)
Missing/unknown	24	12.6	(8.3-18.2)	785	14.5	(13.6-15.5)	769	14.1	(13.1-15.0)
Final outcome									
Survived	164	86.3	(80.6-90.9)	4,568	84.4	(83.4-85.3)	4,349	79.5	(78.4-80.6)
Death (any cause)	9	4.7	(2.2-8.8)	180	3.3	(2.9-3.8)	362	6.6	(6.0-7.3)
Missing/unknown	17	8.9	(5.3-13.9)	667	12.3	(11.4-13.2)	758	13.9	(12.9-14.8)

*95% confidence intervals obtained using the Clopper-Pearson method.

A total of 362 deaths (6.6%; 95%CI: 6.0-7.3) were documented among women diagnosed with COVID-19. Mortality was 4.7% (95%CI: 2.2-8.8) among women with influenza, and 3.3% (95%CI: 2.9-3.8) among those with SARI of unknown etiology. Survival status was missing or unknown for 13%.

Table 4 compares the characteristics of women with COVID-19 who died with the characteristics of survivors. Higher percentages of those who died were aged 30-39 (49.7%; 180/362) and self-identified as *pardo* (53.6%). Hypertension/other cardiovascular diseases, diabetes, and obesity were more common among those who died than among survivors (19.1% versus 9.6%, 16.3% versus 7.4%, and 12.1% versus 4.4%, respectively). Most of the women who died were in the postpartum period (48.3%) or third trimester (29.0%); no information was available about the stage of pregnancy at which they had been infected. Admission to ICU, invasive ventilation, and longer length of ICU stay were also more frequent among those who died.

Table 4. Characteristics of survivors and non-survivors among COVID-19 cases, SIVEP-Gripe, Brazil, January-November 2020 (n=5,469)

Characteristics	Survivors (n= 4,349)		Non-survivors (n=362)		Without outcome* (n=758)	
	n	%	n	%	n	%
Age group (years)						
10 to 19	441	10.1	21	5.8	72	9.5
20 to 29	1,820	41.8	121	33.4	326	43.0

30 to 39	1,771	40.7	180	49.7	313	41.3
40 to 49	317	7.3	40	11.0	47	6.2
Race/ethnicity (self-reported)						
White	1,174	27.0	85	23.5	145	19.1
Black	216	5.0	30	8.3	35	4.6
East Asian	35	0.8	4	1.1	7	0.9
Pardo	2,023	46.5	194	53.6	416	54.9
Indigenous	68	1.6	2	0.5	10	1.3
Missing/unknown	833	19.1	47	13.0	145	19.1
Education level						
No education	9	0.2	2	0.5	6	0.8
Elementary school	557	12.8	40	11.0	107	14.1
High school	1,024	23.5	90	24.9	202	26.6
Higher education	330	7.6	23	6.3	56	7.4
Missing/unknown	2429	55.8	207	57.2	387	51.1
Comorbidities**						
Hypertension or other cardiovascular disease	417	9.6	69	19.1	76	10.0
Diabetes	322	7.4	59	16.3	40	5.3
Asthma or other chronic lung diseases	183	4.2	19	5.2	39	5.1
Obesity	193	4.4	44	12.1	27	3.6
Immunosuppression/HIV	48	1.1	9	2.5	12	1.6
Chronic hematological diseases or anemia	42	1.0	8	2.2	6	0.8
Neurological disease or depression	40	0.9	3	0.8	4	0.5
Chronic kidney disease	27	0.6	6	1.7	13	1.7
Chronic liver disease or hepatitis	13	0.3	3	0.8	1	0.1
Tuberculosis	0	0	2	0.6	0	
Other comorbidities	182	4.2	31	8.6	25	3.3
Smoking (former or current)	13	0.3	1	0.3	5	0.7
Gestational age						
First trimester	304	7.0	12	3.3	62	8.2
Second trimester	770	17.7	61	16.8	154	20.3
Third trimester	2,040	46.9	105	29.0	330	43.5
Trimester ignored	203	4.7	9	2.5	26	3.4
Postpartum or post-abortion	1,032	23.7	175	48.3	186	24.5
Admission to intensive care unit (ICU)						
ICU Length of stay	5 (n=377)	2;10	11 (n=139)	4;19	4 (n=24)	2;15.5
Ventilatory support						
Not artificially ventilated	2,594	59.6	39	10.8	389	51.3
Non-invasive ventilation	1001	23.0	64	17.7	158	20.8
Invasive ventilation	191	4.4	213	58.8	51	6.7
Missing	563	12.9	46	12.7	160	21.1

*Missing or still in hospital.

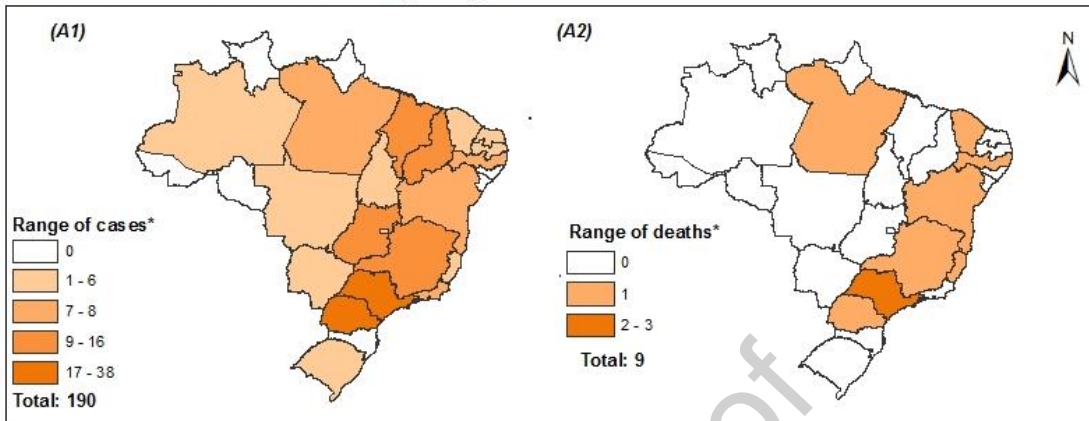
**The sum of the presence of comorbidity may exceed the total of the column, since several comorbidities per woman might apply.

Differences in characteristics were also observed between survivors and non-survivors for other SARIs (Supplementary Tables S3 and S4).

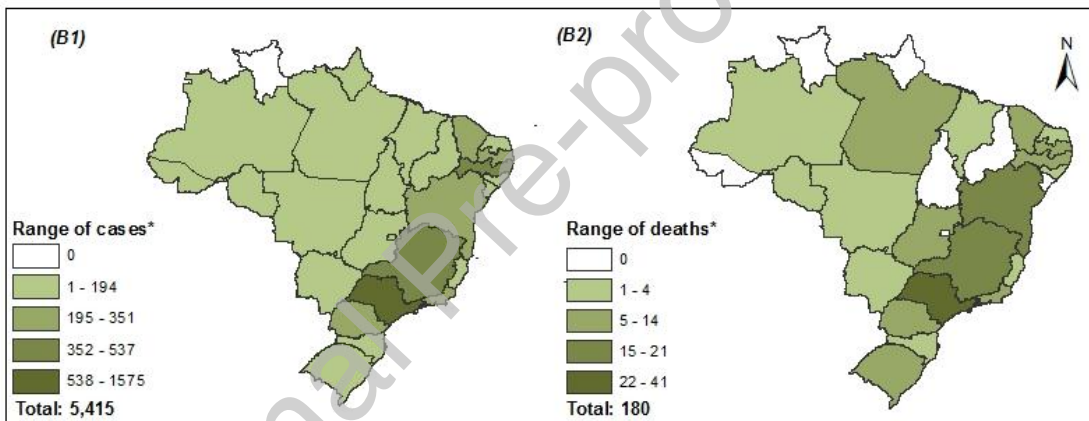
Figure 2 depicts the number of cases and deaths by type of SARI for each of the 27 Brazilian states. Low numbers of cases and deaths were observed for influenza-associated SARI. The absolute numbers of cases of COVID-19 and SARI with unknown etiology were similar, but their geographical distributions differed sharply. The North, Northeast and Central-West regions had higher frequencies of COVID-19 cases and deaths, particularly the Northeast and Southeast states. The supplementary material (Supplementary Tables S5-S7) shows the distribution by region and states for survivors and non-survivors for all SARI types.

Figure 2. Distribution of cases and deaths due to SARIs among pregnant and recently pregnant women, by state, SIVEP-Gripe, Brazil, January-November 2020 (n=11074)

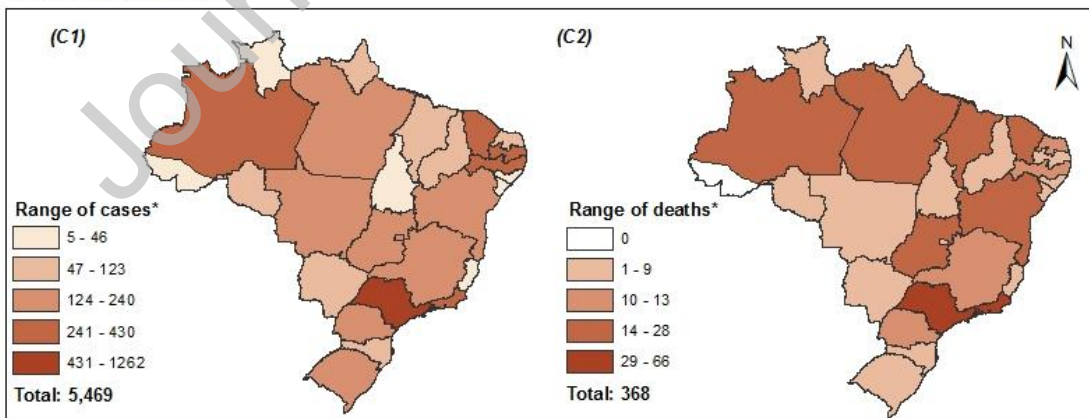
A. SARI with influenza or other etiological agents



B. SARI cases with unknown etiology



C. COVID-19 cases



* Absolute numbers

1:60.000.000
0 420 840 1.680 2.520 3.360 Km

Sistema de Coordenadas Geográficas: SIRGAS, 2000
DATUM: WGS, 1984

Legend: A. SARI with influenza or other etiological agents (A1-Number of confirmed cases; A2-Number of reported deaths). B. SARI cases with unknown etiology (B1-Number of confirmed cases; B2-Number of reported deaths). C. COVID-19 cases (C1-Number of confirmed cases; C2-Number of reported deaths).

Discussion

Using data from a national surveillance system in Brazil, we described the characteristics of pregnant and recently pregnant women with SARIs from January 2020 to November 2020, with special attention to COVID-19, which was confirmed in 50% of the study population. Our inclusion of comparable analyses of the characteristics, outcomes and geographical distribution of pregnancies of SARIs with influenza and those with SARIs of unknown etiology, is an approach, that to our knowledge, has not been previously applied to this population.

Mortality among those with COVID-19 was elevated, compared with the other SARI groups. A total of 362 deaths were recorded among COVID-19 cases. To put this figure in context, 371 maternal SARI deaths were recorded during the 2009-2010 A/H1N1 influenza pandemic, 227 of which were attributed to A/H1N1.¹⁴ COVID-19 mortality in pregnancies is higher in Brazil than estimates from other countries for the same period.⁶

To develop and target public health interventions, it is important to understand why the pandemic is affecting this segment of Brazil's population. Despite substantial improvements, maternal health remains a major concern in LMICs. Morbidity and mortality due to non-communicable and infectious diseases affecting pregnancies are far higher in LMICs than in more affluent countries.¹⁵ Thus, when a pandemic reaches a population already at high risk, the health consequences tend to be greater.

A systematic review has synthesized characteristics of and outcomes for pregnant women affected by COVID-19.⁷ Brazilian authorities are adopting international recommendations, but these guidelines may not reflect the unique characteristics, social context, and health care reality of Brazil. Our study, by contrast, used data from the national surveillance system to focus on pregnant and recently pregnant Brazilian women affected by SARIs.

Age and underlying conditions (notably, chronic hypertension and pre-existing diabetes) have been identified as risk factors for severe COVID-19 in pregnant women.^{6,7} We observed elevated mortality among those with COVID-19 aged 30-39 or who had hypertension/other cardiovascular diseases or diabetes, when compared with their counterparts with other SARIs. However, it was not possible to determine if these conditions were pre-existing or pregnancy-related.

Obesity, another risk factor for unfavorable COVID-19 outcomes, has an estimated prevalence of 18.6% in Brazilian women aged 20 to 49.¹⁶ The prevalence of obesity in our study population was only 5%, but obesity was the third most frequent

comorbidity among women with COVID-19 who died. Because of natural changes in weight associated with pregnancy, this relationship needs to be more carefully quantified.

For cases of SARIs with influenza or other etiological agents, the most common age range for deaths was 20-29, not 30 or older. Also, deaths in this group occurred more frequently among those with asthma or other chronic lung diseases rather than cardiovascular diseases or obesity.

A previous study of mortality among COVID-19 patients, also based on SIVEP-Gripe data, revealed disparities by ethnic/racial group.³ We found similar patterns when the analysis was confined to pregnant and recently pregnant women. In our study, *pardos*, who are concentrated in specific regions,¹⁷ accounted for the largest percentage of infections and deaths. Inequities related to race/ethnicity are well known in Brazil. Whereas 15% of white people live below the poverty line, this is the case for almost 33% of blacks or *pardos*,¹⁸ which may partially explain their lack of access to the health care.^{19,20} Menezes et al.²¹ hypothesized that increased morbidity and mortality are related to lack of access and delays in seeking care. This needs to be considered in evaluations of health care access, particularly access to prenatal care.

Since the 2009 A/H1N1 pandemic, the SIVEP-Gripe has monitored outbreaks in Brazil. However, the data have limitations, including substantial underreporting and poor quality in recording variables such as education, race/ethnicity, and comorbidities. Multiple issues indeed apply with the current system in place for monitoring pregnancies for which no data on pregnancies outcomes are recorded. These shortcomings hinder timely reporting and analyses of infectious disease outbreaks, information that is essential for informed policy-making.

Unlike other countries, Brazil does not have registries or surveillance systems designed to include pregnant and recently pregnant women. In recent months, initiatives have been implemented to monitor health outcomes in women affected by COVID-19 around the world, some of them in Latin America.²² The United Kingdom Obstetric Surveillance System, which aims to describe the epidemiology of a variety of uncommon disorders of pregnancy,²³ now monitors outcomes in women with COVID-19.²⁴ The United States Centers for Disease Control and Prevention has adapted the Surveillance for Emerging Threats to Mothers and Babies Network²⁵ to monitor those affected by COVID-19 and releases weekly reports.²⁶ A European project, "Covid-19 infectiON and medicineS In preGNancy"²⁷ aims to provide guidance to regulators in the management of COVID-19-positive pregnant women. Networks and initiatives like COVI-preg (International COVID-19 and Pregnancy Registry)^{28,29} have been established to determine best practices worldwide.

The results of this study should be considered in the context of several limitations. First, we present only data from the SIVEP-Gripe, which collects information

on hospitalized cases. This yielded a more severely ill study population, and likely generated a higher case fatality rate than would data that included a broader range of clinical severities. The SIVEP-Gripe is not linked with Brazil's surveillance system for mild influenza, influenza-like and Covid-19 cases (e-SUS); linkage would permit assessment of the impact of COVID-19 on a larger, less selective group of pregnant women.

Second, the data were not validated, so misclassification of characteristics of the study population, such as comorbidities or type of SARI, cannot be ruled out. In addition, during the study period, changes occurred in definitions (for example, the use of images in the diagnosis was implemented in August 2020) (Supplementary Table S8).

Third, the SIVEP-Gripe contained no confirmed diagnosis for 1,332 cases, which had to be excluded from the analysis. More specifically, data were missing differentially for underrepresented and vulnerable populations, such as pregnant women and residents of disadvantaged regions.

Fourth, the category "other viral etiologies and co-infection" was ambiguous. If results between laboratory methodologies diverged, the final diagnosis prioritized the RT-PCR and disregarded infections that occurred simultaneously. However, COVID-19 patients can be infected by another respiratory virus, a factor that should be considered when evaluating disease severity.³⁰

Finally, the SIVEP-Gripe does not indicate whether the observed deaths were directly attributed to COVID-19 or other SARIs, or how changes in practice of care and delays in seeking access to care might affect the pregnant population.

Limitations notwithstanding, our analysis has notable strengths. It is one of the few studies based on national surveillance data, and the first to use the SIVEP-Gripe to describe pregnant and recently pregnant women with COVID-19 or other SARIs. We show the absolute burden that COVID-19 imposes on pregnant and recently pregnant women in Brazil.

As previously mentioned, international guidelines for managing pregnancies affected by COVID-19 may not reflect the situation in Brazil. Takemoto et al.⁸ predicted that this would be the case, and our analysis supports their expectation. Our study describes characteristics of women hospitalized with COVID-19 or other SARIs in Brazil and the uneven geographic distribution of these groups. In the effort to avoid more deaths and evaluate the short- and long-term effects of the pandemic, specific regions should be targeted, mainly those where maternal mortality rate is high¹⁵ and where prenatal care is known to be limited.³¹ Projections using previous estimates of live births (Supplementary Figure S1), a proxy for the number of pregnancies, and linkage with the Mortality Information System and the National Live Birth Information System would be beneficial, as would transparent analysis.

In summary, this study provides estimates of maternal morbidity and mortality due to SARIs generally, and COVID-19 specifically, in Brazil. Marked differences in absolute distributions of infections and deaths were observed by region and state. However, higher numbers of reported cases did not necessarily translate into more deaths. Rather, geographic differences were associated with differences in structural socio-economic vulnerability within a diverse, but racialized, country.

The results reinforce the need to collect and rigorously analyze data on trends, possible causes, risk factors, and excess morbidity and mortality in pregnant and recently pregnant women, preferably with governmental support.

Data sharing

SIVEP-Gripe data are publicly available. De-identified and unduplicated individual data are available indefinitely at <https://opendatasus.saude.gov.br/dataset/bd-srag-2020>.

Authors' contributions

LFL, JM, DBF, RK, AEM, WKO, MFS, LA, RWP, and NBB contributed to the conception and design of the study; to the acquisition, analysis, and interpretation of data; and to the draft of the manuscript. LFL and NBB analyzed and reviewed results. All authors have approved the submitted version.

Conflicts of interest

JM is an employee of bioMérieux. The other authors have no competing interests to declare.

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